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Physical inactivity in Parkinson's disease

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Abstract Patients with Parkinson's disease (PD) are likely to become physically inactive, because of their motor, mental, and emotional symptoms. However, specific studies on physical activity in PD are scarce, and results are conflicting. Here, we quantified daily physical activities in a large cohort of PD patients and another large cohort of matched controls. Moreover, we investigated the influence of disease-related factors on daily physical activities in PD patients. Daily physical activity data of PD patients ($n = 699$) were collected in the ParkinsonNet trial and of controls ($n = 1,959$) in the Longitudinal Aging Study Amsterdam (LASA); data were determined using the

LAPAQ, a validated physical activity questionnaire. In addition, variables that may affect daily physical activities in PD were recorded, including motor symptoms, depression, disability in daily life, and comorbidity. Patients were physically less active; a reduction of 29% compared to controls (95% CI, 10–44%). Multivariate regression analyses demonstrated that greater disease severity, gait impairment, and greater disability in daily living were associated with less daily physical activity in PD ($R^2 = 24\%$). In this large study, we show that PD patients are about one-third less active compared to controls. While disease severity, gait, and disability in daily living predicted part of the inactivity, a portion of the variance remained unexplained, suggesting that additional determinants may also affect daily physical activities in PD. Because physical inactivity has many adverse consequences, work is needed to develop safe and enjoyable exercise programs for patients with PD.

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Introduction

Patients with Parkinson's disease (PD) are likely to experience a decrease in their daily physical activity, because of physical impairments, fatigue, and apathy. Such a sedentary lifestyle is undesirable, because physical inactivity is a risk factor for cardiovascular disease, diabetes mellitus, cognitive impairment, osteoporosis, and depression [40]. Moreover, physical inactivity may worsen various non-motor symptoms, such as insomnia and constipation.

Thus far, only a few studies have examined physical activity in PD, and the results were inconsistent. Several

studies found reduced levels of physical activity, but activity levels were not assessed optimally (either indirectly using visual analogous scales [12], or using activity monitors mounted at the wrist, rather than the leg [37]), or studies were very small [5, 35]. Unexpectedly, two studies found that patients and controls spent comparable amounts of time being active [7, 29].

The determinants of physical activity in PD remain incompletely understood [11]. Generic factors such as age [16], gender [6, 16], and health status [16] are associated with the level of physical activity in healthy adults. Furthermore, depression is a risk factor for developing a sedentary lifestyle [30]. Such factors may also affect exercise behavior in patients with PD. Identifying the determinants of physical activity may help to structure new exercise interventions.

Here, we quantified daily physical activities in a large group of PD patients and analyze the associated determinants, using data from the ParkinsonNet trial (699 patients) [24, 25] and the population-based LASA study (1,959 controls) [10].

Methods

Participants

Patients

The ParkinsonNet trial was a cluster randomized trial involving 699 participants that evaluated community-based professional networks of physiotherapists (ParkinsonNet) [24, 25]. Eligibility criteria for patients were the following: (a) PD according to the UK PDS Brain Bank criteria [13]; (b) living independently in the community; (c) <80 years old; (d) able to complete the questionnaires; (e) MMSE >23; and (f) no severe comorbidity interfering with daily functioning. Stage of the disease was scored according to the original Hoehn and Yahr (H&Y) stages [17]. Most patients (81.6%) had moderate disease severity (i.e., H&Y 2–3; Table 1). Mean age was 68.6 ± 7.7 years, 409 patients were men (58.5%), and average disease duration was 5.3 years. Full ethical approval has been granted for the study. All patients signed informed consent. In the study described here, we used baseline data.

Controls

Controls were derived from the Longitudinal Aging Study Amsterdam (LASA), a prospective study of persons aged 55–85 years old (1995–1996) [10]. This cohort forms a nationally representative sample of the older Dutch population and, thus, creates a good control group. After exclusion of participants older than 80 years, data of 1,959

controls were available for the analyses. Mean age was 65.8 ± 7.0 years and 921 subjects were men (47.0%) (Table 1). Full ethical approval has been granted for the study and all respondents gave informed consent at the start of the study.

Daily physical activity in patients and controls

In both groups, daily physical activity was measured with the LASA Physical Activity Questionnaire (LAPAQ) [33]. The LAPAQ covers frequency and duration of different activities during the previous 2 weeks [33, 39]. Activities covered in the LAPAQ include the following: walking outside, cycling, gardening, light and heavy household activities, and a maximum of two sport activities. To consider different levels of intensity of activities, a metabolic equivalent value (MET) was assigned to each activity to calculate the number of kilocalories spent per day per kilogram of body weight [1]. In addition, types of different activities ('inside' and 'outside the house') were specified.

The LAPAQ was initially designed as an interview-based physical activity questionnaire; in the LASA study, data were collected this manner. A self-completed version was used in the ParkinsonNet trial. To reduce recall bias, the time window was limited to 1 week. A random sample of the ParkinsonNet trial population ($n = 76$) completed the questionnaire and was also interviewed similar to the controls. The subgroup was comparable to the total PD population (Table 1).

Disease-related factors associated with daily physical activity in PD

In the ParkinsonNet trial, a wide range of variables were assessed: disease severity (H&Y stages and motor section of the unified Parkinson's Disease Rating Scale [23]), fear of falling (Falls Efficacy Scale-International [34]), anxiety and depression (Hospital Anxiety and Depression Scale [21]), mobility (timed up and go test [22]), freezing of gait (Freezing of Gait questionnaire [14]), walking speed (6-m walk test), disability in daily life (Self-assessment Parkinson's Disease Disability Scale [3]), comorbidity (cumulative illness rating scale [26]), and "faller status" (≥ 1 fall in the preceding year). Patient characteristics included gender, age, education level, and marital status. We studied the influence of these disease-related factors on daily physical activity. We classified six dimensions to analyze all factors: demographics (gender, age, education level, and marital status); health status/disease severity (H&Y, UPDRS, CIRS, and time since diagnosis); walking performance/mobility (TUG, FOGQ, and walking speed); fear of falling, anxiety, and depression (HADS and FES-I); disability in daily life (SPDDS); and faller status.

Table 1 Characteristics of the participants

	Patients		Controls
	Total population	Random sample	
<i>N</i>	699	76	1959
Men	409 (58.5%)	44 (57.9%)	921 (47.0%)
Age	68.6 (± 7.7)	67.6 (± 8.2)	65.8 (± 7.0)
Time since diagnosis	5.3 (± 4.7)	3.9 (± 3.7)	
Education level			
Low	385 (55.1%)	26 (34.2%)	1243 (63.5%)
Medium	112 (16.0%)	16 (21.1%)	367 (18.8%)
High	150 (21.5%)	25 (32.9%)	349 (17.8%)
Missing	52 (7.4%)	9 (11.8%)	0 (0.0%)
Partner			
Yes	522 (74.7%)	54 (71.1%)	1451 (74.1%)
No	131 (18.6%)	13 (17.1%)	508 (25.9%)
Missing	46 (6.7%)	9 (11.8%)	0 (0.0%)
Hoehn & Yahr			
1	77 (11.0%)	7 (9.2%)	
2	327 (46.8%)	36 (47.4%)	
3	243 (34.8%)	25 (32.9%)	
4	34 (4.9%)	7 (9.2%)	
Missing	18 (2.6%)	1 (1.3%)	

Data are mean (SD) or number (%)

Analyses

Data of daily physical activity in both groups were summarized with medians and 25th and 75th percentiles. Since the LAPAQ scores were skewed, linear logarithmic transformation was applied for all subsequent analyses. Differences between patients and controls in minutes per day as well as in kilocalories per day were evaluated using linear regression analyses, with adjustment for gender, age, education level, and marital status. Furthermore, linear regression analysis with forward variable selection was performed to study the association between the dimensions mentioned above and daily physical activities. First, we used a stepwise selection procedure to identify additional variables that contributed significantly. In addition, we used a hierarchic approach whereby in each subsequent step of the selection procedure, an *F* test was performed for each dimension that was not yet in the model. First, the demographic variables were included in the model. The dimension with the smallest *p* value was then included, provided that it was statistically significant. The selection procedure was stopped when the *F* test of none of the remaining dimensions was significant. A two-sided *p* value of <0.05 was considered to indicate statistical significance. In general, selection procedures provide a model, but they do not guarantee that the model is unique. Therefore, we evaluated whether the resulting model was optimal and

unique by calculating the explained variance (R^2) for all possible alternative models.

Results

Daily physical activity in PD compared to controls

Patients spent 111 min/day (interquartile range 58–206) on daily physical activity, compared to 150 min for controls (interquartile range 89–232). This amount led to a 29% reduction in patients versus controls (95% CI, 10–44%; $p < 0.01$). Patients also spent 29% fewer kilocalories during daily physical activity (95% CI, 11–43%; $p < 0.01$). After adjustment for age, gender, education level, and marital status, the difference between patients and controls was 24% (95% CI, 3–40%; $p < 0.05$). In contrast to the control group, the patient population included subjects younger than 55 years of age. Therefore, we performed an additional analysis excluding patients younger than 55 years old, which showed comparable results.

In a subanalysis, we specified the nature of activities. Median time spent to ‘outdoor and sports activities’ did not differ between patients and controls (95% CI, 79–150%). However, PD patients spent significantly less time to activities inside the house (62%; 95% CI, 45–83%; $p < 0.01$).

Table 2 Regression coefficients (%) and 95% confidence intervals for univariate and multivariate analyses between daily physical activities and the explanatory factors

Covariate	Univariate regression (95% CIs)	Multivariate regression
Demographics		
Age (years)	−3 (−5, −2)*	
Gender (women versus men)	80 (44, 125)*	101 (65, 141)
Education level (low, medium, high)	−5 (−17, 9)	
Marital status (partner versus no partner)	6 (−20, 39)	
Health status/disease severity		
H&Y Stage	−34 (−43, −23)*	
UPDRS III (0–108)	−3 (−4, −2)*	
CIRS (0–56)	−28 (−38, −17)*	−18 (−29, −9)
Time since diagnosis (years)	−2 (−4.5, 0.3)	
Walking performance/mobility		
TUG (time in s)	−10 (−13, −8)*	−7 (−10, −4)
FOGQ ^a (0–20)	−19 (−28, −10)*	
Walking speed (speed in m/s)	184 (50, 389)*	
Fear of falling, anxiety and depression		
FES-I ^a (16–64)	−65 (−74, −52)*	
HADS depression (0–21)	−7 (−9, −4)*	
HADS anxiety (0–21)	−4 (−7, −1)*	
Disability in daily life		
SPDDS ^a (24–120)	−82 (−87, −73)*	−63 (−75, −45)
Faller status		
Faller status (no versus yes)	32 (6, 65)*	

H&Y stage Hoehn and Yahr stage, *UPDRS* Unified Parkinson's Disease Rating Scale, *CIRS* cumulative illness rating scale, *TUG* timed up and go test, *FOGQ* freezing of Gait questionnaire, *FES-I* Falls Efficacy Scale-International, *HADS* Hospital Anxiety and Depression Scale, *SPDDS* self-assessment Parkinson's Disease Disability Scale

^a Linear logarithmic transformation was applied; the coefficients presented here indicate the effect of doubling of the score, e.g., when fear of falling increased by a factor 2, daily physical activities decreased by 65%

* Significant relationship between the independent factor and daily physical activities

Disease-related factors associated with daily physical activities in PD

Univariate relationships

Univariate regression analyses were performed to investigate the relation between the various disease-related factors and daily physical activity in minutes per day (Table 2). All disease-related factors were significantly correlated with daily physical activity, except for 'time since diagnosis'. Compared to men, women with PD were 80% more active. Furthermore, time spent on daily physical activity decreased significantly with age (−3% for each year) and with disease severity (−3% for each point on the UPDRS). Figure 1 shows that the time spent on daily physical activity decreased when disease severity increased. In addition, patients without falls in the preceding year spent 32% more

time on daily activity compared to fallers. Greater fear of falling, comorbidity, and depression and anxiety were associated with less daily physical activity in PD.

Multivariate relationships

Stepwise model selection resulted in a model with four variables: gender, comorbidity, mobility, and disability in daily life (Table 2). This model explained 22% of the variance.

However, when we checked whether this model was unique, we found ten additional models leading to 21% explained variance. In addition, the model with three variables (gender, mobility, and disability in daily life) had an explained variance of 21%. All models with five or more variables explained at least 20% of the variance, whereas the percentage explained variance of the full model was 24%. We evaluated the possible collinearity in

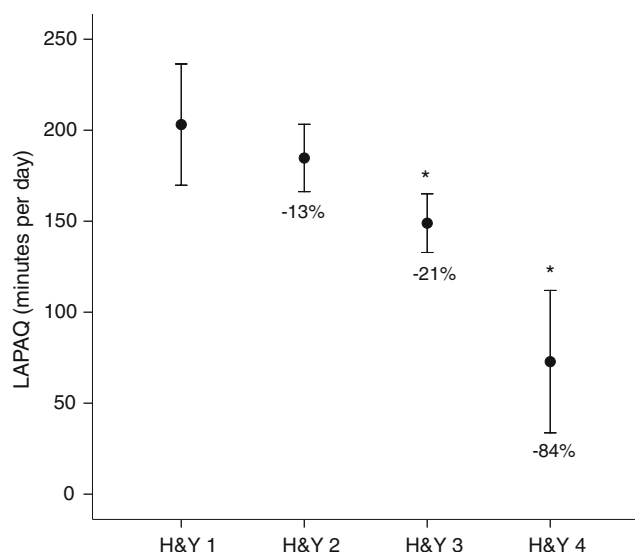


Fig. 1 Levels of daily physical activities per Hoehn & Yahr Stage (H&Y); the error bars reflect the 95% confidence intervals. *decrease is significant compared to H&Y 1

the full model. The largest collinearity index was 3.9 and the largest variance inflation factor (VIF) was 2.6. Only SPDDs and FES-I had a VIF exceeding 2.

Multivariate relationships: hierarchic approach

As we could not find a reasonably unique model in the multivariable approach, we used a hierarchic variable selection to identify dimensions which were associated with daily physical activity. Demographic characteristics were first included in the multivariate regression model and explained a small portion of the variance ($R^2 = 9\%$). The subsequent model selection procedure for dimensions of health resulted in a model with the dimensions walking performance/mobility, disability in daily life, and health status/disease severity. These dimensions, in addition to demographics, jointly explained 24% of the variance in LAPAQ scores (Table 3). Adding more dimensions into the model did not increase the explained variance. This final model was not unique: Table 3

shows that various other models yielded only slightly lower R^2 .

Discussion

Patients with PD are widely presumed to follow a sedentary lifestyle, due to their physical, cognitive, and emotional impairments. We now provide new evidence to underpin this assumption, based on analyses of time spent on daily physical activity in a large cohort of PD patients and another large cohort of controls. The loss of time spent on activities was most obvious in patients with greater disease severity.

Our results showed that PD patients were 29% less active compared to controls. In a previous study of 24,000 subjects aged 65 years and older, similarly reduced activity levels (by about 23%) were found for patients with a chronic disease such as musculoskeletal disorders and vascular or heart diseases [2]. The 29% reduction observed for PD patients in the present study might even be greater in comparison with healthy controls since our cohort did not include severely affected PD patients [24]. Moreover, the LASA study, which we used as a control group, showed that about 60% of the population had a chronic disease [39]. Direct comparison for comorbidity between the two groups was not possible as the LASA study only recorded broad categories and did not subdivide in specific disorders. Although it would be interesting incorporating fall histories in the analysis, data of fall history was not available for the control group. Future studies are required to investigate the influence of these factors.

It is important to consider the methods used to assess physical activity in the present and other studies. We used a validated interview-based physical activity questionnaire [33], which is a subjective method of measuring physical activity. This might have resulted in an overestimation of the reported physical activity. However, this possible overestimation likely applies equally to both patients and controls, so it is unlikely that this influenced our results. Another possibility is that patients underestimated their

Table 3 Models with their explained variance (R^2); all models were adjusted for demographic characteristics

One dimension	R^2 (%)	Two dimensions	R^2 (%)	Three dimensions	R^2 (%)
ADL	19	Walking, ADL	23	Severity, walking, ADL	24
Walking	18	Severity, ADL	21	FoF & anxiety, walking, ADL	23
Severity	15	Severity, walking	20	Walking, falls, ADL	23
Falls	15	FoF & anxiety, ADL	20	Severity, FoF & anxiety, ADL	22
FoF & anxiety	10	Falls, ADL	19	Severity, falls, ADL	21

Classified dimensions: *Severity* Health status/disease severity, *Walking* walking performance/mobility, *FoF & anxiety* fear of falling, anxiety and depression, *ADL* disability in daily life, *Falls* faller status

activity due to memory problems. However, patients with severe cognitive impairment (MMSE < 24) were excluded, so this is unlikely to explain the physical inactivity observed in PD patients. Other studies circumvented such problems by using objective measures of physical activity; these studies did not find differences between patients and controls [7, 11, 37]. Although these activity monitors have been well validated and shown to be reliable for a range of activities, some specific activities such as gardening and cycling are difficult to quantify [9, 20, 41]. This may be one reason for the discrepancy with our results.

We also investigated the determinants associated with daily physical activity in PD patients. One factor was gender. Univariate regression analysis showed that women with PD were 80% more active than men. This is in contrast with observations in non-PD populations [16]. The LAPAQ assessed a broad range of activities, including walking outside, cycling, gardening, light and heavy household activities, and a maximum of two sport activities. When we removed the household activities from the total activity score, men appeared to be more physically active than women ($p < 0.01$). The same effect was found in the control group. This suggests that women spent more time to daily activities because the LAPAQ records household activities. Another study found comparable results for older women: two-thirds of them reached recommended levels of physical activity when domestic activities were included in the assessment, but only 21% when these domestic activities were excluded [19].

We also found several additional determinants associated with daily physical activity. Specifically, inactivity in PD was associated with worse walking performance, more disability in daily life, and greater disease severity. These factors identified in this study for PD are comparable to other studies that investigated the determinants of physical inactivity in older persons [2, 6, 32].

Our results concerning the determinants of daily physical activity in PD have to be interpreted with some caution for several reasons. First, the final model was not unique, because various different combinations of determinants yielded almost the same percentage of explained variance. A model with two dimensions (i.e., walking performance and disability in daily life) was as good as a model with three dimensions (additionally including either disease severity, fear of falling, anxiety and depression, or faller status).

Second, in all models, the unexplained variance remained large. Our final model explained 24% of the variance. Adding more variables into the model did not increase the explained variance. This suggests that additional factors are responsible for the variability in LAPAQ scores in PD. Because we secondarily analyzed data from two previous trials, various factors were not investigated. One such factor is fatigue, which may be an independent

contributor to physical inactivity in PD [11]. Moreover, social cognitive theories propose that behavioral factors are associated with physical activity [28, 32]. Earlier work showed that a model which included self-efficacy and outcome expectations, explained 64% of the variance in exercise behavior in older adults [28]. Other studies found that (lack of) interest in physical activity, knowledge about the benefits of exercise, and social supports also predicted exercise behavior [8, 28, 32]. In the literature, many other possible determinants have been suggested, ranging from income and socioeconomic status up to seasonal effects [30, 31, 36]. Further work, therefore, remains necessary to identify ‘all’ determinants, as a basis for future therapeutic interventions.

Although we showed that physical inactivity was most obvious in patients with greater disease severity, not all PD patients with advanced disease were completely sedentary. This suggests that even PD patients in later stages of the disease might be stimulated to become more active. Participating in regular physical activity would be particularly useful for PD patients, because exercise may help to prevent cardiovascular events, diabetes mellitus, and osteoporosis [40]. Moreover, in older subjects, physical activity was reported to suppress typical PD symptoms such as depression and cognitive decline [4, 18]. In addition, pre-clinical evidence in animals with experimental parkinsonism suggests that exercise may directly alter the neurodegenerative process in PD [27]. A meta-analysis found exercise to be effective at improving physical functioning, health-related quality of life, strength, balance, and gait speed for people with PD [15]. It is, therefore, important for PD patients to avoid a sedentary lifestyle. Simply informing people about the health benefits of physical activity is likely insufficient to attain a sustained behavioral change. Motivational aspects are especially important because such behavioral interventions could target motivation to increase levels of physical activity. We are now testing this in the ParkFit trial, a large exercise study involving 586 PD patients randomized to receive a behavioral change program aimed to increase daily physical activity levels. The ParkFit trial uses motivational strategies and personal health coaches to induce a lasting increase in exercise behavior for patients with PD; the first results are expected in 2012 [38].

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Conflict of interest The authors declare that they have no conflict of interest.

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